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Review

Preventing the onset of post traumatic stress disorder

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ABSTRACT

Post-traumatic stress disorder (PTSD) is a common mental health condition that requires exposure to a traumatic event. This provides unique opportunities for prevention that are not available for other disorders. The aim of this review was to undertake a systematic review and evaluation of randomized controlled trials (RCTs) of interventions designed to prevent PTSD in adults. Searches involving Cochrane, Embase, Medline, PsycINFO, PILOTS and Pubmed databases were undertaken to identify RCTs of pre-incident preparedness and post-incident interventions until May 2019. Six pre-incident and 69 post-incident trials were identified that could be included in meta-analyses. The overall quality of the evidence was low. There was emerging evidence that some interventions may be helpful but an absence of evidence for any intervention that can be strongly recommended for universal, selected or indicated prevention before or within the first three months of a traumatic event. The strongest results were found for cognitive-behavioural therapy with a trauma focus (CBT-T) in individuals with a diagnosis of acute stress disorder which supports calls to detect and treat individuals with significant symptoms rather than providing blanket preventative interventions. Further research is required to optimally configure existing interventions with some evidence of effect and to develop novel interventions to address this major public health issue.

1. Introduction

1.1. Background

Posttraumatic stress disorder (PTSD) is a common mental condition associated with significant distress and impaired functioning (NICE, 2018; Olff et al., 2019). Although there has been some divergence between the latest versions of the main classification systems (ICD-11 (WHO, 2018) and DSM-5 (APA, 2013)), key inclusion criteria for both are exposure to a major traumatic event and characteristic symptoms including re-experiencing, avoidance and increased sense of threat. DSM-5 has broadened the definition of PTSD and incorporated a new symptom cluster of "altered cognitions and mood associated with the traumatic event". ICD-11 has narrowed the definition, making PTSD primarily fear-based. The extant prevention literature almost totally relies on the DSM definition of PTSD, primarily the DSM-IV definition (APA, 1994).

The lifetime incidence of exposure to traumatic events with the potential to precipitate PTSD is estimated to be over 50% in the general population with the incidence of PTSD estimated to be in the order of 3–7% (Kessler et al., 2017; McManus, Meltzer, Brugha, Bebbington, & Jenkins, 2008). Recent studies suggest that CPTSD may be slightly more common than PTSD (Cloitre et al., 2019; Karatzias et al., 2019). Although the majority of people exposed to traumatic events do not develop PTSD, certain traumatic events, particularly those of an interpersonal nature, are associated with a particularly high rate of PTSD development (Atwoli, Stein, Koenen, & McLaughlin, 2015; Kilpatrick et al., 2013).

It is postulated that early intervention following a traumatic event has the potential to prevent the development of PTSD. A number of

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different theoretical paradigms have been suggested, including the memory consolidation framework (Pitman, 2019), emotional processing theory (Foa & Kozak, 1986) and the cognitive theory of PTSD (Ehlers & Clark, 2000). How best to intervene soon after a traumatic event to prevent PTSD has become something of a holy grail for practitioners and researchers although results to date have not been as encouraging as would have been hoped (Roberts, Kitchiner, Kenardy, Lewis, & Bisson, 2019). There has also been an increasing interest in delivering preventative interventions before traumatic events occur to high risk populations such as military personnel (e.g., Riggs & Sermanian, 2012). As for other forms of prevention, there are a number of possible approaches to the prevention of PTSD. Within public health, a universal, selective and indicated classification system (Gordon, 1983) is often advocated and this will be used to highlight possible approaches to the prevention of PTSD.

1.2. Types of prevention

A *universal* prevention strategy addresses the entire population under consideration. Public health approaches to prevent traumatic events occurring and providing psychoeducational messages through the media to unselected populations both pre- and post-incident such as everyone exposed to a particular traumatic event would be examples of a universal approach. It can be argued that only interventions aimed at the entire population should be considered universal (Magruder, Kassam-Adams, Thoresen, & Olff, 2016) but a slightly broader interpretation is adopted in this review. *Selective* prevention targets groups of the total population at risk. For example, this would include an intervention delivered to people who lived within a certain radius from the site of an explosion or only to individuals with known low social support. *Indicated* prevention is designed to prevent the onset of PTSD in individuals who do not meet DSM or ICD criteria but are showing early symptoms.

1.3. The existing evidence

A heterogeneous range of pharmacological and psychosocial approaches have been evaluated to prevent PTSD. A number of systematic reviews and meta-analyses have been undertaken and used to synthesize the evidence and develop recommendations for the prevention of PTSD in recently published guidelines (ISTSS, 2018; NICE, 2018; VA/DoD, 2017). Roberts, Kitchiner, Kenardy, Lewis, and Bisson (2019) identified 61 randomized controlled trials (RCTs) of multiple session psychological interventions designed to prevent or treat symptoms of PTSD within three months of a traumatic event. No evidence was found to support any intervention for universal prevention but people reporting traumatic stress symptoms at the start of intervention (indicated prevention) did significantly better with cognitive-behavioural therapy with a trauma focus (CBT-T), cognitive therapy and eye movement desensitization and reprocessing (EMDR). There was also evidence that CBT-T interventions designed to provide early treatment to people with PTSD were effective (e.g., Ehlers et al., 2003; Öst, Paunovic, & Gillow, unpublished; Shalev et al., 2012). Astill Wright et al. (2019) found limited evidence for the pharmacological prevention or early treatment of PTSD. Of 19 RCTs identified, covering seven different pharmacological agents, only hydrocortisone was found to be superior to placebo. Given the nature of the RCTs included and potential adverse effects, the authors expressed caution with respect to the clinical use of hydrocortisone to prevent PTSD before further research.

The prevention recommendations of the recently updated International Society for Traumatic Stress Studies PTSD Prevention and Treatment Guidelines (International Society for Traumatic Stress Stuides (ISTSS), 2018) were informed by the results of the Roberts, Kitchiner, Kenardy, Lewis, and Bisson (2019) and Astill Wright et al. (2019) meta-analyses, along with unpublished meta-analyses concerning single session psychological interventions designed to prevent PTSD. The ISTSS guidelines recommended CBT-T, cognitive therapy and EMDR for the early treatment of people with symptoms of PTSD within three months of a traumatic event. They also noted emerging evidence for hydrocortisone, group 512 PM (an enhanced form of group psychological debriefing), single-session EMDR, brief dyadic therapy, and a self-guided internet-based intervention. The United Kingdom's National Institute for Health and Care Excellence's recently updated guidelines (NICE, 2018) recommended against offering psychologically-focused debriefing or drug treatments for the prevention of PTSD and to offer an individual CBT-T intervention to adults who have acute stress disorder or clinically important symptoms of PTSD within a month of a traumatic event. The United States' Department of Veterans Affairs and Department of Defense guidelines made no recommendations for universal or indicated prevention of PTSD, except for people with a diagnosis of acute stress disorder (ASD), when "individual trauma-focused psychotherapy that includes a primary component of exposure and/or cognitive restructuring" is recommended (VA/DoD, 2017).

1.4. The present review

The aim of this paper is to review and synthesize the RCT evidence currently available for the universal and indicated prevention of PTSD and to describe the clinical and research implications of this. This has been achieved by updating systematic reviews and meta-analyses used to inform the ISTSS guideline recommendations and undertaking a systematic review and meta-analysis of RCTs that have focused on pre-incident preparedness to prevent PTSD. To facilitate interpretation, the results of the reviews and meta-analyses conducted have been separated into the following groups: pre-incident preparedness; single session early interventions; multiple session early interventions; and pharmacological interventions.

2. Methods

2.1. Data sources

2.1.1. Pre-incident preparedness

A search was undertaken using the CENTRAL (Cochrane), Medline, PsycINFO and Published International Literature on Traumatic Stress (PILOTS) databases to identify RCTs of pre-incident preparedness interventions to cover the period Jan 2008 to May 2019. The following search terms were used: PTSD or "post-traumatic stress disorder" or "posttraumatic stress disorder" or "post traumatic stress disorder" AND preparedness OR pre-incident OR inoculation OR prevent* OR resilien*OR protect* OR pre-trauma OR pretrauma OR plan* AND intervention OR training OR program OR trial.

2.1.2. Post-incident interventions

This review built on systematic reviews previously undertaken by the review team using the same methodology (Bisson, Andrew, Roberts, Cooper, & Lewis, 2013; Hoskins et al., 2015; Lewis, Roberts, Bethell, & Bisson, 2015; Roberts, Kitchiner, Kenardy, & Bisson, 2009, Roberts, Kitchiner, Kenardy, & Bisson, 2010; Rose, Bisson, Churchill, & Wessely, 2005; Sijbrandij, Kleiboer, Bisson, Barbui, & Cuijpers, 2015). Studies had previously been identified to 2008. Following on from the previous searches, a systematic computerized literature search of the Cochrane Common Mental Disorders Group clinical trials registers databases was undertaken. The search was designed to identify studies concerning the prevention and treatment of PTSD published from January 2008 to May 2016, with updated searches in March 2018 and May 2019, using the search terms PTSD or posttrauma* or post-trauma* or 'post trauma*' or 'combat disorder*' or 'stress disorder*'. The searches included results from PubMed, PsycINFO, Embase and the Cochrane database of randomized trials.

Reference lists of the included studies were checked and the World Health Organization's, and the U.S. National Institutes of Health's trials portals searched to identify additional unpublished or ongoing studies.

Table 1
Study inclusion criteria.

- Any RCT (including cluster and crossover trials) evaluating the efficacy of interventions aimed at preventing PTSD.
- Study participants have been exposed to a traumatic event, as specified by PTSD diagnostic criteria for DSM-III, DSM-III-R, DSM-IV, DSM-5, ICD-9, ICD-10, or ICD-11 (not required for pre-incident preparedness studies).
- Intervention begins no later than 3 months after the traumatic event (not required for pre-incident preparedness studies).
- Eligible comparator interventions for psychosocial interventions: waitlist, treatment as usual, symptom monitoring, repeated assessment, other minimal-attention control group, or an alternative psychological treatment.
- Eligible comparator interventions for pharmacological interventions: placebo, other pharmacological or psychosocial intervention.
- The RCT is not solely a dismantling study (i.e. the intervention being evaluated needs to be complete).
- Study outcomes include a standardised measure of PTSD symptoms (either clinician-administered or self-report).
- Individual, group, and couple interventions.
- Adults aged 18 and over only. In cases where there were a combination of adults and adolescents, at least 80% of the sample had to be 18 or over.
- No minimum sample size.
- Only studies published in English.
- Unpublished studies eligible.

Experts in the field were contacted with the aim of identifying unpublished studies and studies that were in submission. Complementary searches of the PILOTS database were also conducted. A list of studies identified in the original search were posted on the website of the ISTSS and its membership asked to identify studies that might have been missed. The searches were originally undertaken to support development of new PTSD treatment guidelines for the ISTSS (Bisson et al., 2019) and Australia (Phoenix Australia, 2020).

2.2. Study selection

Study abstracts were read independently by two of the reviewers to determine if they potentially met the inclusion criteria. The full manuscripts of all studies that either reviewer felt potentially met the criteria were obtained and read independently by two reviewers to determine if the inclusion criteria (see Table 1) were met.

2.3. Data extraction

A data extraction sheet was designed to capture data which was then entered into Review Management 5 (RevMan-5.3) software (Cochrane Collaboration, 2014). Information extracted included demographic details of participants, inclusion and exclusion criteria, details of the traumatic event, the randomization process, the interventions used, drop-out rates and outcome data. Study quality was assessed with the Cochrane Collaboration's tool for assessing risk of bias (Higgins et al., 2011) using the domains: sequence generation, allocation concealment (selection bias), blinding of assessors (detection bias), incomplete outcome data (attrition bias), selective outcome reporting, and other sources of bias. For pharmacological interventions, blinding of participants and personnel (performance bias) was also assessed. Data were extracted and quality assessed by two reviewers independently. Any disagreements were discussed with a third reviewer and a consensus achieved.

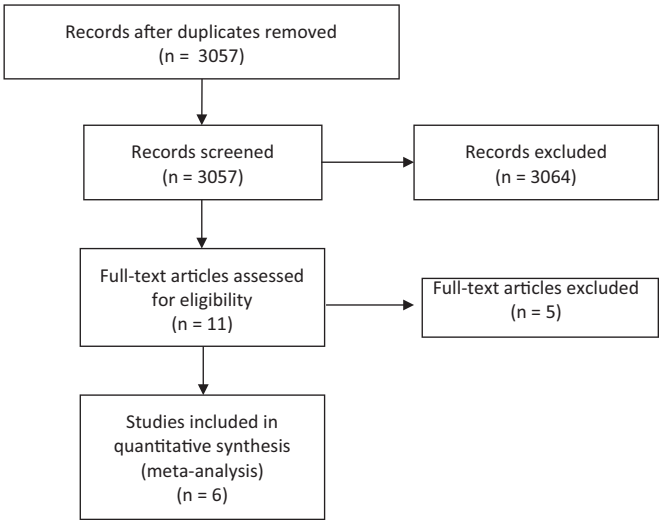

Fig. 1. PRISMA study flow diagram for pre-incident preparedness.

2.4. Data synthesis

Trials were initially separated into four groups: pre-incident preparedness; single session early interventions; multiple session early interventions; and pharmacological interventions. The primary outcome was PTSD symptom severity. When an individual study reported both a clinician-administered and a self-report measure, primacy was given to outcomes using the clinician-administered measure. Self-report measures were used if no clinician-administered measure was used. PTSD diagnosis was the other outcome of interest.

The interventions were grouped into the categories defined by the ISTSS Guidelines Committee (a multi-disciplinary committee with expertise across the full range of psychological and pharmacological approaches used to prevent PTSD). The categories were believed by the committee to "be widely recognised as separate by the traumatic stress community and allow discrimination between different types of intervention" (ISTSS, 2018). Interventions were grouped according to their broad theoretical base (e.g., CBT-T and EMDR) and, when possible, subgroups were developed to allow more detailed consideration of specific interventions within a theoretical grouping (e.g., prolonged exposure and cognitive therapy). In addition, novel groupings were developed for interventions that did not fit into established groupings, e.g., "brief individual trauma processing therapy". Description of the intervention groupings are included in Tables 3, 5, 7 and 9 below, alongside summaries of the meta-analysis results.

Data were analyzed for summary effects using the Review Manager 5.3 program (Cochrane Collaboration, 2014). All continuous outcomes were analyzed using standard mean differences (SMD), in order to compare effects across analyses. SMD assumes that all scales are measuring the same underlying symptom or condition. Relative risk was calculated for diagnostic status. 95% confidence intervals were calculated for all outcomes. Available case analysis and (for relative risk) intent to treat analysis with imputation using the last observation carried forward method were performed when enough information was available. In cases where there was inadequate information within the paper to perform these analyses further information was requested from the lead author.

Heterogeneity between studies was assessed by considering the I^2 and chi^2 test of heterogeneity. This statistic measures the percentage of variation that is not due to chance (Fletcher, 2007). An I^2 of less than 30% was taken to indicate mild heterogeneity and a fixed effects model was used. When the I^2 was greater or equal to 30% a random-effects model was used. A visual inspection of the forest plots was used as a test of robustness of these findings. It was decided a priori that if a minimum of 10 studies were available in a meta-analysis, funnel plots would be prepared and examined for signs of asymmetry. Where asymmetry was indicated, other possible reasons for this were considered.

The quality of evidence was assessed using the 'Grades of Recommendation, Assessment, Development, and Evaluation' (GRADE) approach (Guyatt, Oxman, Schünemann, & Tugwell, 2001; Guyatt, Oxman, Sultan, Brozek, et al., 2013). GRADE considers five factors: limitations in study design and implementation of available studies,

Table 2
Description of studies included in pre-incident intervention meta-analyses.

Pre-incident Interventions										
Study	Country	Number	Intervention(s)	Control	Time before trauma	Trauma exposure	Outcome measure	Follow-up period	Significant differences	Risk of bias ratings* ABCDEF
Hourani et al. (2016)	USA	263	Stress inoculation training	Stress management	Pre-deployment	Combat	PCL-C	Post 7 month deployment	NS	UUUHHH
Hourani et al. (2018)	USA	267	Stress inoculation training	Stress management	Pre-deployment	Combat	PCL-C (baseline) PCL-M (follow-up)	18 months from baseline training	NS	UUUHUH
Pyne et al. (2019)	USA	307	Heart Rate variability cognitive bias feedback	No intervention	Pre-deployment (within 12 months)	Combat	PCL-M	3 months post-deployment	NS	UUUHUH
Skeffington, Rees, Mazzucchelli, and Kane (2016)	Australia	61	MAPS resilience training	No intervention	First week of recruit school	fire and emergency services	PCL-C	6 months post baseline	NS	LLUUUU
Wald et al. (2016)	Israel	587	Attention Bias modification training (4 or 8 sessions) attention control therapy	No intervention	Basic training	Combat	PCL-M	4 months following combat	Favors ABMT	LLLLUL
Wald et al. (2017)	Israel	99	Single session attention bias modification training	ACT	Pre-deployment	Combat	PCL	2 months	NS	UUUHUH

Note. ABMT = Attention Bias Modification Training; ACT = Attention Control Training; PCL-M = PTSD Checklist – Military; PCL-C = PTSD Checklist – Civilian; MAPS = Moment, Assess, Plan, Support.* Risk of bias judgements for each study (in six domains: A = random sequence generation; B = allocation concealment; C = incomplete data; D = blinding of assessors; E = selective reporting; F = other bias) are graded **L** = low risk; **U** = unclear risk; **H** = high risk).

Table 3
Summary results of pre-incident intervention meta-analyses.

Intervention	Description of intervention	Summary result versus TAU/WL (number of studies; number of participants; standardised mean difference and 95% confidence intervals)	GRADE judgment for quality of evidence
Attention bias modification training	A dot-probe task that was designed to shift participants'attention toward threat (i.e. targets always appeared at the threat word location).	k = 1; *N* = 308; SMD −0.15, CI −0.37 to 0.08	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Attention control training	A dot-probe task designed to balance attention deployment between neutral and threat words rather than to shift attention patterns.	k = 1; *N* = 297; SMD −0.16, CI −0.39 to 0.07	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Cognitive bias modification for interpretation	This intervention promotes less negative appraisals of post-event retrospections rather than modifying attention to prospective combat threats. The iMAT (Mental Armour training) software presents emotionally ambiguous deployment-related scenarios (2–3 sentences) until the last word, which over time increased in neutral or non-negative interpretations of the scenario. The last work is presented as a word fragment, which the participant is asked to complete.	k = 1; *N* = 215; SMD −0.16, CI −0.44 to 0.12	Very uncertain about the estimate.
Heart Rate Variability (HRV) Biofeedback	Uses an earlobe sensor device and software to detect heart rhythm and calculate HRV. This informs game-based HRV training where a series of progressively more challenging games are controlled by the user's HRV.	k = 1; *N* = 227; SMD −0.23, CI −0.49 to 0.04	Very uncertain about the estimate.
MAPS resilience training	A psychoeducation program focusing on strength, mental health, wellbeing, and normalizing coping.	k = 1; *N* = 61; SMD 0.41, CI −0.1 to 0.92	Very uncertain about the estimate.
Stress Inoculation Training (SIT)	A resilience-building, breathing training intervention that consists of education, skills acquisition, and practice in a simulated environment. HRV-assisted biofeedback was used to support SIT and monitor autonomic arousal.	No data available	

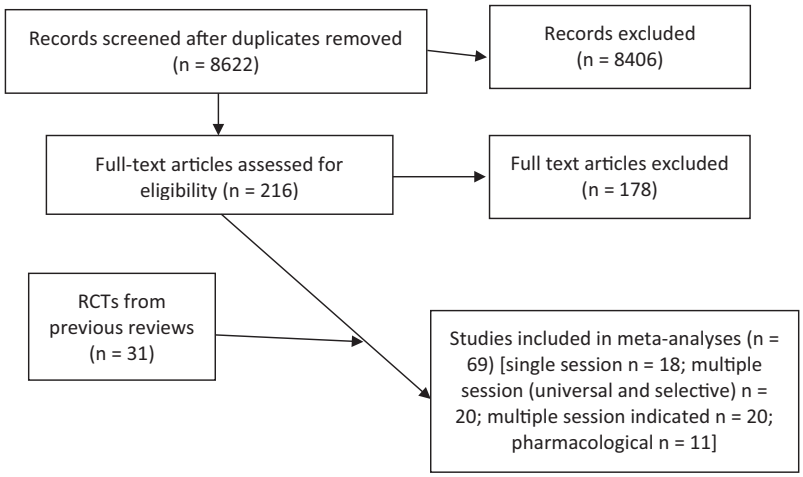

Fig. 2. PRISMA Study Flow Diagram for Post-incident Interventions.

indirectness of evidence, unexplained heterogeneity or inconsistency of results, imprecision of effect estimates, and potential publication bias. The quality of evidence for each comparison was graded according to confidence that the estimate of effect would remain unchanged as a result of further research. A high rating indicates that further research is very unlikely to change confidence in the estimate of effect; a moderate rating indicates that research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate; low quality indicates that further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate; very low quality indicates that the estimate of effect is very uncertain.

3. Results

3.1. Pre-incident preparedness

The PRISMA study flow diagram (Fig. 1) shows the number of studies considered and included in the pre-incident preparedness meta-analyses described below.

Table 2 summarizes the six studies included in the meta-analyses and Table 3 provides the summary results for the six interventions included in meta-analyses compared to no intervention with respect to PTSD symptoms following exposure to a traumatic event. All interventions included were universal interventions as they targeted the entire population under consideration. As shown in Table 2, the majority of the studies included significant risk of bias. No intervention prevented PTSD symptoms (the primary outcome) significantly more than receiving nothing/usual care. Attention bias modification training (ABMT) did fare better than a no training control for the prevention of PTSD (K = 1; *N* = 360; RR 0.32, CI 0.10 to 0.97) (Wald et al., 2016) but this was the only statistically significant difference found for any comparisons.

There were no significant differences for direct comparisons between ABMT and attention control training (ACT) (K = 1; *N* = 364; SMD 0.02, CI −0.21 to 0.25) (Wald et al., 2016); single session ABMT and ACT (K = 1; *N* = 99; SMD 0.19, CI −0.20 to 0.59) (Wald et al., 2017); heart rate variability feedback and cognitive bias modification for interpretation (K = 1; *N* = 172; SMD −0.06, CI −0.36 to 0.24) (Pyne et al., 2019); or stress inoculation training and stress management (K = 1; *N* = 267; SMD 0.01, CI −0.23 to 0.25) (Hourani et al., 2018).

3.2. Post-incident interventions

The PRISMA study flow diagram shows the number of studies considered and included in the single session psychosocial interventions, multiple session psychosocial interventions and pharmacological interventions meta-analyses described below (Fig. 2).

3.2.1. Single session psychosocial interventions

Table 4 shows the individual studies and Table 5 and Figs. 3-5 provide summary results and forest plots of the meta-analyses for the interventions considered versus no intervention. The majority of interventions were universal; Scholes, Turpin, & Mason, 2007, Gil-Jardiné et al., 2018 and Jarero & Artigas, 2011 were indicated. As can be seen from the results in Table 4, the majority of the studies included significant risk of bias. Single session EMDR and Group 512 PM did better than receiving nothing/usual care in preventing the development of PTSD symptoms at the follow up point closest to three months after the traumatic event (for single session EMDR this was 2–5 days following the intervention which was targeted at people with early symptoms). There were major concerns about the quality of the studies and risk of bias for both the single session EMDR and Group 512 PM studies included, leading to GRADE ratings of being very uncertain about the effect estimates found.

No significant difference was found between no intervention and any other intervention considered but small numbers of studies and participants, along with methodological weaknesses concerning randomization, blinding of assessors, incomplete outcome data, fidelity checking and time of post-intervention assessment meant uncertainty around the estimates, even for single session individual psychological debriefing, the most researched single session early intervention (meta-analysis shown in Fig. 3). Table 5 and Fig. 4 show that the meta-analysis results for group psychological debriefing, although not significant, appear more positive than for individual PD and Table 5 and Fig. 5 suggest a greater effect than either for Group 512 PM (Psychological Intervention Model), a variant of group psychological debriefing with cohesion training being an integral component. Indeed, a head to head comparison of Group 512 PM and group psychological debriefing showed significant advantage to the former (K = 1; *N* = 379; SMD −0.42; CI −0.57 to −0.27) (Wu et al., 2012). In the other head to head comparisons, EMDR was superior to group debriefing (K = 1; *N* = 41; SMD −4.43, CI −5.62 to -3.25) (Tarquinio et al., 2016); there was no difference between EMDR and reassurance (k = 1, *n* = 72; RR 0.19; CI 0.02 to 1.47) (Gil-Jardiné et al., 2018); and no difference between trauma-focused counselling and heart stress counselling (k = 1, *n* = 183; RR 2.84; CI 0.12 to 68.86) (von Känel et al., 2018).

3.3. Multiple session psychosocial interventions (universal and selective)

Table 6 shows the individual studies and Table 7 and Fig. 6 provide summary results and a forest plot of the meta-analyses for the interventions considered versus no intervention. As can be seen from

Table 4
Description of studies included in single session intervention meta-analyses.

Single session interventions										
Study	Country	Number	Intervention(s)	Control	Time since trauma	Trauma exposure	Outcome measure	Follow-up period	Significant differences (in favor of)	Risk of bias [a]ABCDEF
Adler et al. (2008)	USA	614	Group debriefing, Group stress management	Usual care	End of tour of duty	Military peacekeepers	PCL	3–4 months	NS	UHUHUU
Bisson, Jenkins, Alexander, and Bannister (1997)	UK	103	Individual debriefing	Usual Care	2–19 days	Acute burn trauma	CAPS	3 months	NS	L LULLH
Conlon, Fahy, and Conroy (1999)	Ireland	40	Individual debriefing	Advice leaflet	3–14 days	Motor vehicle accident	IES	3 months	NS	LHUUUH
Dolan, Bowyer, Freeman, and Little (1999)	UK	100	Individual debriefing	Usual Care	7–11 days	Life-threatening experiences	IES	6 months	NS	UUUUUU
Freedman, Eitan, and Weiniger (2020)	Israel	55	Computerized visuospatial task	Usual care	Less than 8 h	Physical injury	PSS	6 months	NS	ULLHHU
Gil-Jardiné et al. (2018)	France	109	EMDR, reassurance	Usual care	3	Physically injured in ER with risk	PTSD	3 months	NS	UHUHHH
Hobbs, Mayou, Harrison, and Worlock (1996)	UK	91	Individual debriefing	Advice leaflet	1–2 days	Motor vehicle accident	IES	4 months	NS	LUUHUH
Horsch et al. (2017)	Switzerland	56	Computerized visuospatial task	Usual care	Less than 6 h	Caesarian Section	PDS	1 month	NS	LLULHU
Iyadurai et al. (2018)	UK	71	Computerized visuospatial task	Attention-placebo	Less than 6 h	Physical injury	PDS	1 month	NS	LLLLLH
Jarero, Artegas, and Luber (2011)	Mexico	18	EMDR	Wait list	3 weeks	Earthquake with risk	IES	4 days	EMDR	UHULHH
Lee, Slade, and Lygo (1996)	UK	39	Individual debriefing	Usual care	2 weeks	Miscarriage	IES	4 months	NS	UHUUHH
Rose, Brewin, Andrews, and Kirk (1999)	UK	105	Individual debriefing education only	Usual care	Maximum one month	Violent crime	PSS	11 months	NS	LLUHLL
Scholes et al. (2007)	UK	120	Individual psychoeducation/ self-help	Usual care	Maximum one month	A&E attenders at risk	PDS	3 months	NS	ULLHUH
Tarquinio et al. (2016)	France	60	EMDR, individual debriefing	Wait list	48 h	Workplace violence	PCL	48 h	EMDR	UUULHH
Tuckey and Scott (2014)	Australia	67	Group debriefing, Group education	Usual care	Within 3 days	Firefighters post events	IES-R	3–4 months	NS	LHUUHU
Turpin, Downs, and Mason (2005)	UK	142	Individual psychoeducation/ Self-help	Usual care	Within 6–8 weeks	Injury attending ER	PDS	6 months	NS	ULLHUU
von Känel et al. (2018)	Switzerland	183	Trauma-focused counselling	Heart Stress Counselling	2 days	Myocardial infarction	CAPS	3 months	NS	LHULLH
Wu et al. (2012)	China	1130	512 PM group debriefing	Usual care	Median 25 days	Earthquake – military rescuers	SI-PTSD	4 months	512 PM Group debriefing	UUUUUU

[a] Risk of bias judgements for each study (in six domains: A = random sequence generation; B = allocation concealment; C = incomplete data; D = blinding of assessors; E = selective reporting; F = other bias) are graded **L** = low risk; **U** = unclear risk; **H** = high risk).

Table 6, the majority of the studies included significant risk of bias. Most interventions were universal. Gidron et al., 2001 and Gidron et al., 2007 (raised heart rate required), Brunet, Des Groseilliers, Cordova, & Ruzek, 2013 and Marchand et al., 2006 (peritraumatic fear, helplessness or horror required) and Rothbaum et al., 2012 (fear of death or serious injury required) were selective. The only interventions that were found to be superior to receiving nothing/usual care in preventing the development of PTSD symptoms were brief dyadic therapy and self-guided internet-based CBT. There were concerns about the quality of the studies and risk of bias for both, leading to GRADE ratings indicating significant uncertainty around the estimates of effect.

No significant difference was found between no intervention and any other intervention considered but the small numbers of studies and participants, along with methodological weaknesses concerning randomization, blinding of assessors, incomplete outcome data, power and fidelity checking meant uncertainty around all the estimates. Several studies evaluated interventions which although theoretically diverse had some common key components, which included psychoeducation, therapist directed reliving of the index trauma to promote elaboration of the trauma memory and help to contextualize or reframe aspects of the experience; these approaches were grouped as brief individual trauma processing therapy. Brief individual trauma processing

Table 5
Summary results of single session intervention meta-analyses.

Intervention	Description of intervention	Summary result versus TAU/WL (number of studies; number of participants; standardised mean difference and 95% confidence intervals)	GRADE judgment for quality of evidence
Individual psychological debriefing	Individuals are asked to provide detailed facts of what happened, their thoughts, reactions and symptoms before being provided with psychoeducation about symptoms and how to deal with them.	k = 6; *N* = 427; SMD 0.09, CI -0.1 to 0.28	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Group psychological debriefing	As above but in a group format.	k = 3; *N* = 1184; SMD -0.09, CI -0.2 to 0.03	Very uncertain about the estimate.
Group stress management	Education and skills training in techniques aimed at controlling/ reducing levels of stress.	k = 1; *N* = 411; SMD -0.08, CI -0.28 to 0.11	Very uncertain about the estimate.
Computerized visuospatial task	This involves playing a computer game (e.g.Tetris) to disrupt consolidation of trauma memories.	k = 3; *N* = 182; SMD -0.21, CI -0.51 to 0.08	Very uncertain about the estimate.
Group 512 PM	Group 512 PM is based on debriefing but supplemented with cohesion training exercises, for example playing games that need team co-operation.	k = 1; *N* = 758; SMD -0.54, CI -0.68 to −0.39	Very uncertain about the estimate.
Group Education	Provision of psychoeducational information in a classroom setting.	k = 1; *N* = 47; SMD 0.20, CI -0.39 to 0.78	Very uncertain about the estimate.
Individual Psychoeducation/ self-help	Provision of psychoeducational information in booklet or leaflet form.	k = 3; *N* = 272; SMD -0.05, CI -0.28 to 0.19	Very uncertain about the estimate.
EMDR	Standardised, eight-phase, trauma-focused therapy, involving the use of bilateral physical stimulation (eye movements, taps or tones).	k = 2; *N* = 55; SMD -3.47, CI -4.35 to −2.59	Very uncertain about the estimate.

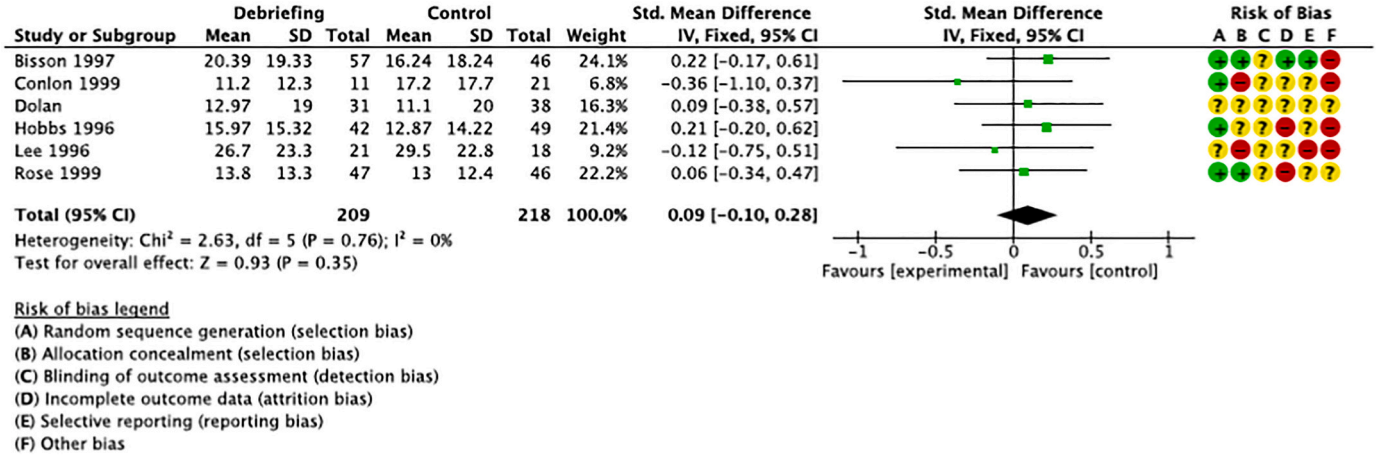

Fig. 3. Individual psychological debriefing forest plot of PTSD severity 3-6 M post trauma.

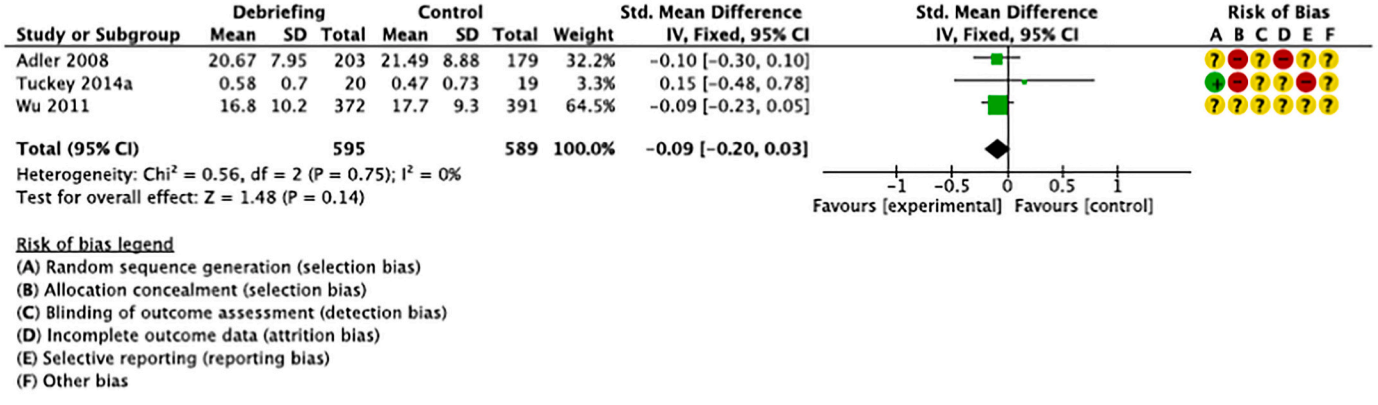

Fig. 4. Group psychological debriefing forest plot of PTSD severity 3-6 M post trauma.

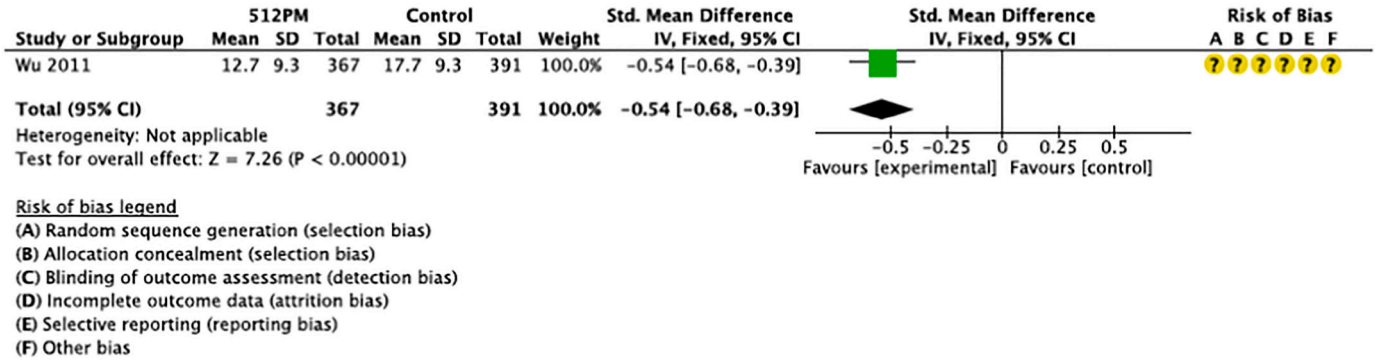

Fig. 5. Group 512 PM forest plot of PTSD severity 3-6 M post trauma.

therapy was the most researched multiple session preventative intervention (meta-analysis shown in Fig. 6). Head to head comparisons showed no significant difference between brief individual trauma processing therapy and supportive listening (K = 2; *N* = 51; SMD −0.54, CI −1.42 to 0.34) or parenting support (K = 1; *N* = 239; SMD 0.06, CI −0.019 to 0.31). No difference was found between guided self-help and physical educational intervention (K = 1; *N* = 175; SMD 0.13, CI −0.16 to 0.43).

3.4. Multiple session psychosocial interventions (indicated)

Table 8 shows the individual studies and Table 9 and Figs. 7 and 8 provides summary results and forest plots of the meta-analyses for the interventions considered versus no intervention. The majority of the studies included significant risk of bias and the GRADE ratings demonstrates significant uncertainty with respect to the effect estimates. CBT with a trauma focus, brief EMDR, internet based guided self-help and stepped/collaborative care were found to be superior to receiving nothing/usual care in preventing the development of PTSD symptoms.

No other intervention was found to be superior to receiving nothing/usual care but small numbers of studies and participants, along with methodological weaknesses concerning randomization, blinding of assessors, incomplete outcome data, power and fidelity checking meant uncertainty around the estimates. CBT-T and stepped/collaborative care had the most robust evidence although further research would still be very likely to change the estimates (meta-analyses shown in Figs. 7 and 8). Head to head comparisons found CBT-T to have a positive effect over supportive counselling (k = 8; *n* = 331; SMD −0.61; CI −1.01 to −0.22) (meta-analysis shown in Fig. 9). The CBT-T in six of these studies was a brief prolonged exposure-based intervention and a sub-group analysis yielded similar results (k = 6; *n* = 262; SMD −0.78; CI −1.26 to −0.30).

CBT-T was superior to supportive counselling (k = 7; *n* = 271; SMD −0.70; CI −1.13 to −0.27). Brief CPT was not significantly different to supportive counselling (k = 2; *n* = 69; SMD −0.17; CI −0.64 to 0.30) (Nixon, 2012; Nixon et al., 2016). No difference was found between CBT-T and a self-help program (k = 1; *N* = 37; SMD −0.39; CI −1.04 to 0.26) (Wu, Li, & Cho, 2014). Structured writing therapy showed no benefit over psychoeducation (k = 1; *n* = 104; SMD 0.16; CI −0.23 to 0.55) (Bugg, Turpin, Mason, & Scholes, 2009). Computerized neurobehavioral training was not significantly different to computerized games control condition (k = 1; *n* = 59; SMD −0.17; CI −0.69 to 0.35), or reading tasks (k = 1; *n* = 49; SMD −0.09; CI −0.71 to 0.53) (Ben-Zion et al., 2018). Prolonged exposure-based intervention was no different to cognitive therapy (k = 1; *n* = 60; SMD −0.41; CI −0.93 to 0.1) (Bryant et al., 2008).

3.5. Pharmacological

Table 10 shows the individual studies and Table 11 the summary results of the meta-analyses for the interventions considered versus no intervention. Nine studies were universal while two were selective; two propranolol studies required participants to have a heart rate of >80 (Hoge, Worthington, Nagurney, et al., 2012; Pitman, Sanders, Zusman, et al., 2002). The majority of the studies again included significant risk of bias and the GRADE ratings demonstrate significant uncertainty with respect to the effect estimates. Hydrocortisone was the only medication found to be superior to placebo in preventing the development of PTSD symptoms at the follow up point closest to three months after the traumatic event.

No significant difference was found between placebo and any other intervention considered but small numbers of studies and participants, along with methodological weaknesses concerning randomization, blinding of assessors, incomplete outcome data, power and follow-up timings meant marked uncertainty around the estimates, including for the hydrocortisone estimate. There was some additional evidence to support hydrocortisone when considering the outcome of presence of PTSD at the point nearest to three months after the traumatic event (k = 3, *n* = 88; RR 0.21; CI 0.05 to 0.89) (Delahanty, Gabert-Quillen, Ostrowski, et al., 2013; Weis, Kilger, Roozendaal, et al., 2006; Zohar, Yahalom, Kozlovsky, et al., 2011). Relative risk analyses for other medications were not superior to placebo.

4. Discussion

Despite the inclusion of 75 RCTs that have explored the efficacy and effectiveness of various approaches to prevent PTSD in adults, the results of this review paint a disappointing picture with respect to the prevention of PTSD. This is consistent with other recent reviews (Astill Wright et al., 2019; Roberts, Kitchiner, Kenardy, Lewis, & Bisson, 2019) and the recommendations contained within recent guidelines (VA/DoD, 2017; NICE, 2018; ISTSS, 2018; Phoenix Australia, 2020). There is emerging evidence that some interventions may be helpful but an absence of evidence for any intervention that can be strongly recommended for universal, selected or indicated prevention before or within the first three months of a traumatic event. In common with results of meta-analyses for the treatment of PTSD (Lewis, Roberts, Andrew, Starling, & Bisson, 2020), interventions with a trauma focus appear to facilitate better outcome.

In terms of pre-incident preparedness, none of the interventions evaluated made a significant difference to our primary outcome although ABMT's superiority over no training with respect to PTSD diagnosis, in a study of ABMT delivered to infantry soldiers prior to combat deployment (Wald et al., 2016), suggests it is a candidate for further development and evaluation. For single session early interventions, the picture for individual psychological debriefing has not advanced for many years with evidence of an absence of effect on meta-analysis considering PTSD symptoms 3–6 months after the traumatic event (Rose et al., 2005). The picture, however, appeared different for psychological debriefing delivered to homogeneous groups (the use for which it was originally developed; Mitchell, 1983) with this meta-

Table 6
Description of studies included in multiple session psychosocial intervention (universal and selective) meta-analyses.

Multiple session psychosocial interventions – universal and selective										
Study	Country	Number	Intervention(s)	Control	Time Since trauma at start	Trauma exposure	Primary Outcome measure	Follow-up period	Significant differences	Risk of bias ratings[a] ABCDEF
Als, Nadel, Cooper, Vickers, and Garralda (2015)	UK	23	Supported psychoeducational intervention	TAU/UC	7 days post discharge	Parents of children admitted to PICU	IES	3–6 months post discharge	NS	LLLHLH
Borghini et al. (2014)	Switzerland	55	Perinatal parenting intervention	TAU/UC	33 weeks post conception	Mothers of infants born before 33 weeks gestation on NICU	PPQ	4 months post corrected infant birth	NS	ULUHUU
Brom, Kleber, and Hofman (1993)	Netherlands	151	Brief individual trauma processing therapy	TAU/UC	Circa 1 month	MVA	IES	6 months	NS	UUHHUH
Brunet et al. (2013)	Canada	74	Brief dyadic CBT intervention	Waiting list	Within 30 days	Life threatening event	CAPS	Post-intervention	NS	LUULUH
Cox et al. (2018)	USA	175	Telephone based CBT	Physical education	Post discharge	Mechanical ventilation on ICU > 48 h	IES-R	3 months post-treatment	NS	LLLLLH
Curtis et al. (2016)	USA	168	Communication facilitator in an intensive care setting	UC	During ICU stay	Family members of patients on ITU	PCL	6 months post discharge or death	NS	LLLHLU
Gamble et al. (2005)	Australia	103	Brief individual trauma processing therapy	TAU	Within 72 h of childbirth	Traumatic childbirth	MINI-PTSD	3 months post birth	Favors intervention	LLULUU
Gamble, 2010	Australia	239	Brief individual trauma processing therapy	Parenting support	72 h post birth	Traumatic childbirth/ Emergency CS	PDS	6 months	NS	LUUHLH
Gidron et al. (2001)	Israel	17	Brief individual trauma processing therapy	Supportive listening	24 h	MVA and heart rate > 95	PDS	3–4 months	Favors intervention	UHLHUH
Gidron et al. (2007)	Israel	34	Brief individual trauma processing therapy	Supportive listening	Within 48 h	MVA and heart rate > 95	PDS	3 months	NS	UULHHH
Holmes et al. (2007)	Australia	58	Brief IPT	TAU	Screening at 2 weeks	Major physical trauma	PCL	6 months	NS	LLLHUU
Irvine et al. (2011)	Canada	185	Telephone based CBT	TAU	Unclear	ICD transplant surgery	IES-R	6 months	NS	LULLLU
Jensen et al. (2016)	Denmark	215	Nurse-led intensive care recovery program	TAU	1–3 months post discharge	Mechanical ventilation on ICU	HTQ-IV	12 months	NS	LLUHLH
Jones (2010)	Multiple	322	Intensive care diary	TAU (received diary at 3 months)	During ICU stay	ICU stay >72 h	PDS-IV	3 months post discharge	NS	LLHLUH
Kazak et al. (2005)	USA	29	Brief dyadic CBT intervention	TAU	Median 6 days	Parents of children with new cancer diagnosis	IES-R	2 months post treatment	NS	ULLHUH
Marchand et al. (2006)	Canada	75	Brief individual trauma processing therapy	TAU	2–22 days after robbery	Armed robbery	IES,	3 months post baseline	NS	UULLUU
Mouthaan et al. (2013)	Netherlands	300	Internet based CBT	TAU	1 week	Suspected severe physical injury	CAPS	6 months post injury	Favors intervention	LLLLLH
Rothbaum et al. (2012)	USA	137	Brief individual trauma processing therapy	TAU	72 h	DSM-IV criterion A event attending ED	PSS-I	12 weeks	NS	LLLUUH
Ryding, Wijma, and Wijma (1998)	Sweden	99	Brief individual trauma processing therapy	TAU	During inpatient stay	Emergency Caesarian Section	IES	6 months	NS	HHLLUU
Zatzick et al. (2001)	USA	26	Collaborative Care	TAU	During inpatient stay	Injured MVA and assault victims	PCL-C	4 months	NS	ULLLUH

[a] Risk of bias judgements for each study (in six domains: A = random sequence generation; B = allocation concealment; C = incomplete data; D = blinding of assessors; E = selective reporting; F = other bias) are graded **L** = low risk; **U** = unclear risk; **H** = high risk).

analysis almost achieving statistical significance in favor of group debriefing.

512 PM, an adaptation of group debriefing to include work to promote cohesion with military personnel in China (Wu et al., 2012) fared best of all universal interventions with significant superiority over both usual care and group debriefing in its standard form. Cohesion and social support have been identified as protective against PTSD (Brewin, Andrews, & Valentine, 2000) and this, along with the early promise of 512 PM suggest it is an approach that could be usefully further explored. Our results would not support a recommendation for the use of any form of psychological debriefing but would also not support NICE's recommendation against the use of any form of psychological debriefing (NICE, 2018).

Single session EMDR also fared better than usual care or group debriefing in small, methodologically weak studies that need replicating in better designed studies. Despite considerable interest in interventions with a consolidation mechanism (Iyadurai, 2018), computerized visuospatial tasks such as Tetris did not achieve significance in reducing the risk for PTSD symptoms. In addition to absence of effect, possible explanations include their primary target being on intrusive memories rather than on all symptoms of PTSD, and, in common with many other interventions considered, possible suboptimal configuration or delivery

Table 7
Summary results of studies multiple session psychosocial intervention (universal and selective) meta-analyses.

Intervention	Description of intervention	Summary result versus TAU/WL (number of studies; number of participants; standardised mean difference and 95% confidence intervals)	GRADE judgment for quality of evidence
Brief individual trauma processing therapy	Diverse therapies with common components of psychoeducation, therapist directed reliving of the index trauma to promote elaboration of the trauma memory and help to contextualize or reframe aspects of the experience.	k = 4; *N* = 466; SMD −0.05, CI −0.41 to 0.30	Very uncertain about the estimate.
Perinatal parenting intervention	Primarily focused on supporting the interaction between the neonate and mother post premature birth.	k = 1; N = 55; SMD −0.08, CI −0.61 to 0.45	Very uncertain about the estimate.
Brief dyadic CBT intervention	CBT based therapies delivered dyadically with the aim of improving communication and fostering a shared approach to addressing psychological and practical difficulties.	k = 2; *N* = 103; SMD −0.41, CI −0.81 to −0.02	Very uncertain about the estimate.
Internet based CBT	Internet-based programs to treat PTSD sufferers using CBT-T approaches. Often guided by a therapist who has less contact with the patient than in traditional face-to-face CBT-T.	k = 1; *N* = 300; SMD −0.27, CI −0.50 to −0.04	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Brief Interpersonal Psychotherapy (IPT)	Attachment-based treatment that focuses on current interpersonal problems and the resolution of these to improve symptoms.	k = 1; *N* = 58; SMD 0.10, CI −0.42 to 0.61	Very uncertain about the estimate.
Intensive care diaries	Provision of post discharge diary feedback following intensive care unit admission to help promote an understanding of events that occurred.	k = 1; *N* = 322; SMD 0.00, CI −0.22 to 0.22	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Stepped/Collaborative care	Flexible and modular interventions based on needs identified through screening and direct assessment. Normally CBT based, but sometimes based on other psychological approaches (e.g. motivational interviewing) and may include components of case management and medication.	k = 1; N = 26; SMD 0.41, CI −0.37 to 1.19	Very uncertain about the estimate.
Supported psychoeducational intervention	Provision of psychoeducational information, normally in booklet or leaflet form, with follow-up guidance, typically by telephone, aimed at reinforcing use of the psychoeducational material.	k = 1; N = 23; SMD −0.35, CI −1.28 to 0.59	Very uncertain about the estimate.
Telephone based CBT	CBT delivered by telephone, rather than face-to-face.	k = 1; *N* = 185; SMD −0.20, CI −0.49 to 0.09	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Communications facilitator in an intensive care setting	Aims to understand the needs of patients and their families in an intensive care setting and active liaison between clinicians and patients and family members in order to improve communication and expectations.	k = 1; *N* = 168; SMD 0.02, CI −0.29 to 0.32	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Nurse-led intensive care recovery program	Nurse led psychological intervention aimed at developing a narrative about the individual's admission and stay on an intensive care unit.	k = 1; N = 215; SMD −0.02, CI −0.29 to 0.25	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.

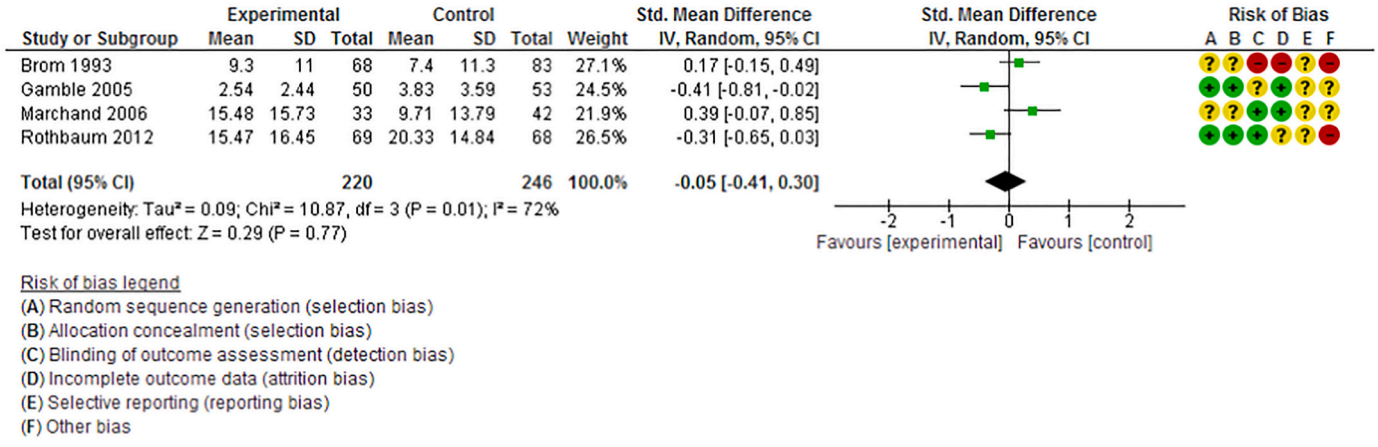

Fig. 6. Brief individual trauma processing therapies versus intervention as usual, waiting list or no intervention.

of the interventions considered.

Universal and selective multiple session preventative interventions also yielded disappointing results with only brief dyadic therapy and self-guided internet-based CBT demonstrating some weak evidence of effect and these results need replicating. The results for indicated multiple session preventative interventions were better although not as strong as for early treatment trials that have treated people diagnosed PTSD within three months of the traumatic event (Roberts, Kitchiner, Kenardy, Lewis, & Bisson, 2019; Ehlers et al., 2003; Öst et al., unpublished; Shalev et al., 2012). The strongest results were found for CBT-T in

Table 8
Description of studies included in multiple session psychosocial intervention (indicated) meta-analyses.

Multiple session psychosocial interventions - indicated										
Study	Country	Number	Intervention(s)	Control	Time since trauma	Trauma exposure	Outcome measure	Follow-up period	Significant differences	Risk of bias ratings[a]ABCDEF
Ben-Zion et al. (2018)	Israel	73	Computerized neurobehavioral training	Computerized games reading tasks	At least 7 days	Physical injury	CAPS NS	6 months	NS NS	UUUHHH
Bisson, Shepherd, Joy, Probert, and Newcombe (2004)	UK	152	Brief PE based	Usual Care	5–10 weeks	Physical injury	CAPS	3 months	NS	LLLLUH
Bryant, Harvey, Basten, Dang, and Sackville (1998)	Australia	24	Brief PE based	Supportive counselling	Mean 10 days	MVA or industrial accident with ASD	IES	6 months	Favors intervention	UULUUH
Bryant, Sackville, Dang, Moulds, and Guthrie (1999)	Australia	45	Brief PE based	Supportive counselling	10 days	MVA or non sexual assault with ASD	CAPS	6 months	Favors intervention	UULHUH
Bryant, Moulds, Guthrie, and Nixon (2003)	Australia	24	Brief PE based	Supportive counselling	2 weeks	Mild TBI from MVA or non sexual assault with ASD	CAPS	6 months	Favors intervention	LULLUH
Bryant, Moulds, Guthrie, and Nixon (2005)	Australia	42	Brief PE based	Supportive counselling	2 weeks	MVA or non sexual assault with ASD	CAPS	6 months	Favors intervention	LULLUH
Bryant et al. (2008)	Australia	60	Brief PE based brief cognitive therapy	Wait list	Mean 22.8 days	MVA or non sexual assault with ASD	CAPS	6 months	Favors interventions	LLLUUH
Bugg et al. (2009)	UK	104	Structured writing therapy	Psychoeducation	5–6 weeks	Civilian trauma with ASD	PDS	6 months	NS	LLLHUH
Cernvall, Carlbring, Ljungman, Ljungman, and von Essen (2015)	Sweden	58	Internet and CBT based guided self help	TAU	Not reported	MVA, occupational injury or assault injury - ED	PCL-C	Post treatment	Favors intervention	LLLHUH
Freedman, unpublished	Israel	139	Telephone based CBT	Wait list	16 days	MVA	CAPS	3 months post treatment	NS	UULULU
Freyth, Elsesser, Lohrmann, and Sartory (2010)	Germany	40	Brief PE based	Supportive counselling	20.5 days	Various trauma with ASD	IES-R	3 months post treatment	NS	HHLHUH
Jarero et al. (2011)	Mexico	18	Brief EMDR	Waiting list	16 days	Earthquake survivors	IES	Post treatment	Favors intervention	LLULUH
Jarero, Uribe, Artigas, and Givaudan (2015)	Mexico	25	Brief EMDR	Waiting list	25 days	Factory explosion	SPRINT	Post treatment	Favors intervention	LLUUUH
Nixon, 2012	Australia	23	Brief CPT based	Supportive counselling	4 weeks	Assault survivors with ASD	CAPS	6 months	NS	LULHUH
Nixon et al. (2016)	Australia	46	Brief CPT based	Supportive counselling	4 weeks	Sexual assault survivors with ASD	CAPS	6 months	NS	UULHUH
O'Donnell et al. (2012)	Australia	42	Stepped/collaborative care	TAU	4 weeks	Physically injured MVA and assault victims	CAPS	6 months post baseline	Favors intervention	LLLLUU
O'Donnell et al. (unpublished)	Australia	61	Telephone based CBT-T	TAU	4 weeks	Physically injured MVA, accident or assault	CAPS	6 months post injury	NS	LLLLLU
Shaw et al. (2013)	USA	98	Brief CBT-T based	TAU	2 weeks	Mothers of premature infants with ASD depression, anxiety or acute distress	DTS	Post treatment	NS	LULLLL
Wu et al. (2014)	Hong Kong	37	Brief PE based	Self-help program	Baseline 1 month	MVA victims presenting to ED with TSS	IES-R	6 months	NS	LHLHUH
Zatzick et al. (2004)	USA	102	Stepped/collaborative care	TAU	Soon after admission	Physically injured hosp'd MVA & assault victims	PCL	6 months	NS	LLULUL
Zatzick et al. (2015)	USA	121	Stepped/collaborative care	TAU	During admission	Physically injured hosp'd	PCL	6 months	NS	LLLLLL

[a] Risk of bias judgements for each study (in six domains: A = random sequence generation; B = allocation concealment; C = incomplete data; D = blinding of assessors; E = selective reporting; F = other bias) are graded **L** = low risk; **U** = unclear risk; **H** = high risk).

Table 9
Summary Results of Multiple Session Psychosocial Intervention (Indicated) Meta-analyses.

Intervention	Description of intervention	Summary result versus TAU/WL (number of studies; number of participants; standardised mean difference and 95% confidence intervals)	GRADE judgment for quality of evidence
CBT with a trauma. Focus	Therapies that aim to help early traumatic stress symptoms by addressing and changing thoughts, beliefs and/or behavior. Typically, CBT-T involves homework and includes psycho-education, exposure work, cognitive work and more general relaxation/stress management; the relative contribution of these elements varies between different forms of CBT-T.	k = 4; *N* = 273; SMD −0.49, CI −0.93 to −0.05	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.
Cognitive therapy	Focuses on the identification and modification of negative appraisals and behaviors that lead to overestimates of current threat (fear). It also involves modification of beliefs related to other aspects of the experience and how the individual interprets their behavior during the trauma (e.g. issues concerning guilt and shame).	k = 1; N = 60; SMD −0.50, CI −1.01 to 0.00	Very uncertain about the estimate.
Brief EMDR	Standardised, eight-phase, trauma-focused therapy, involving the use of bilateral physical stimulation (eye movements, taps or tones).	k = 2; *N* = 43; SMD −4.17, CI −5.53 to −2.80	Very uncertain about the estimate.
Internet based guided self help	Internet-based programs to treat PTSD sufferers using CBT approaches with self-direction.	k = 1; N = 58; SMD −0.66, CI −1.19 to −0.13	Very uncertain about the estimate.
Telephone based CBT-T	CBT-T delivered by telephone, rather than face-to-face.	k = 2; *N* = 191; SMD −0.06, CI −0.22 to 0.35	Very uncertain about the estimate.
Stepped/ collaborative care	Flexible and modular interventions based on needs identified through screening and direct assessment. Normally CBT based, but sometimes based on other psychological approaches (e.g. motivational interviewing) and may include components of case management and medication.	k = 3; *N* = 370; SMD −0.45, CI −0.65 to −0.24	Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate.

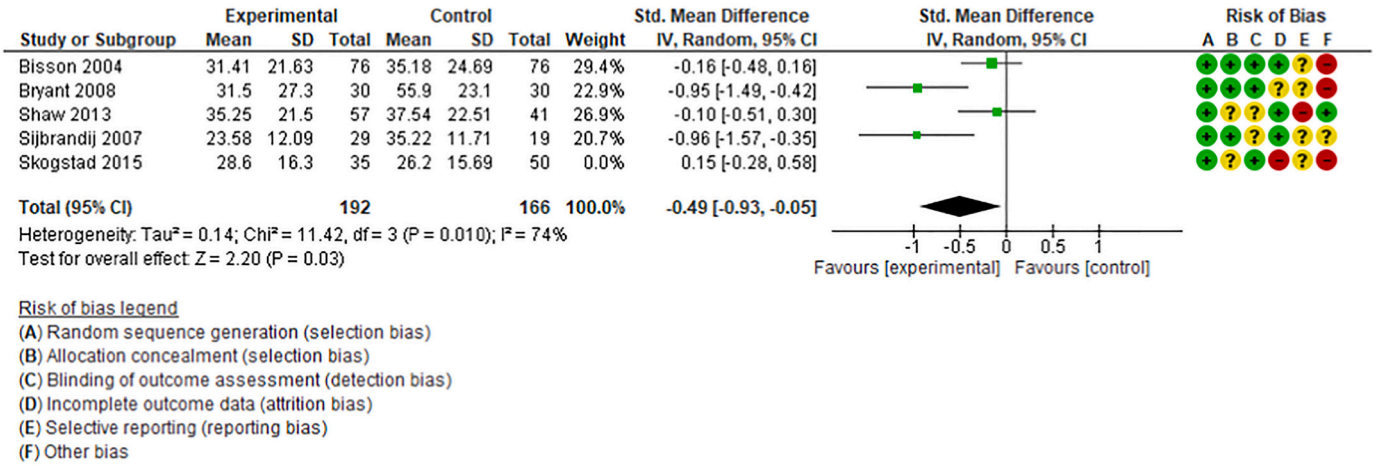

Fig. 7. CBT with a trauma focus (CBT-T) vs WL/ TAU.

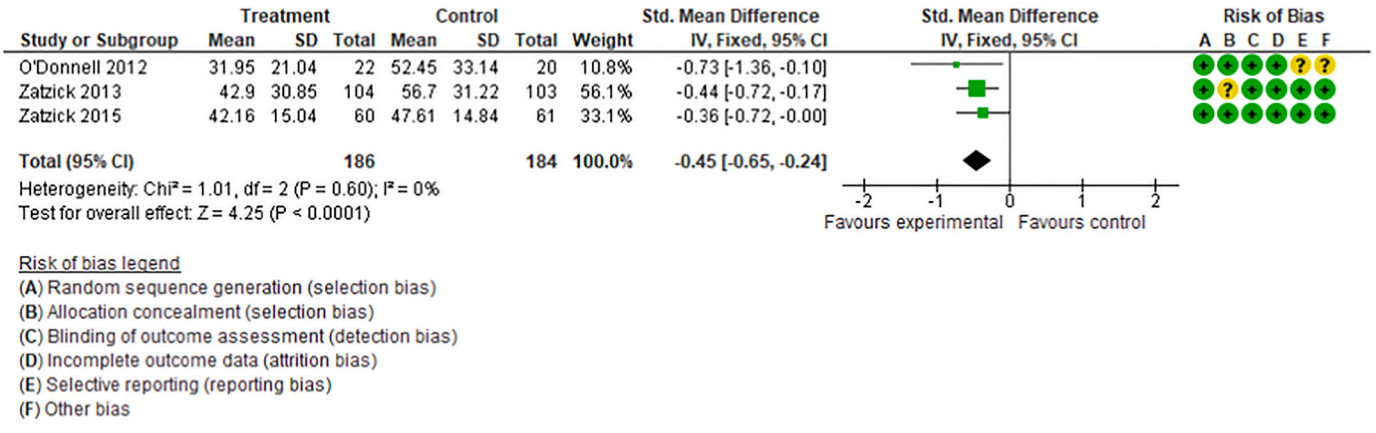

Fig. 8. Stepped/collaborative care versus vs WL/ TAU.

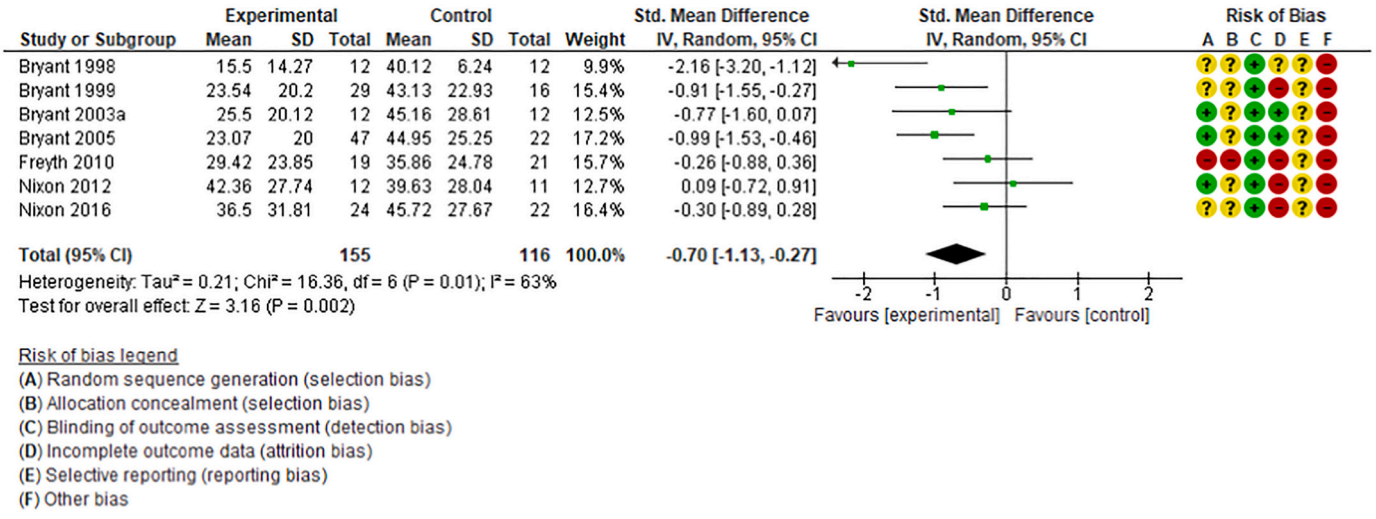

Fig. 9. *CBT with a trauma focus* vs supportive counselling.

Table 10
Description of studies included in pharmacological intervention meta-analyses.

Pharmacological interventions									
Study	Country	Number	Intervention(s)	Time since trauma	Trauma exposure	Outcome measure	Follow-up period	Significant differences	Risk of bias ratings[a] ABCDEFG
Delahanty et al. (2013)	USA	43	Hydrocortisone	<12 h	Injury	CAPS	3 months	Hydrocortisone favored	UULUHUH
Denke, Deja, Carstens, and Sprung (2008)	Germany	18	Hydrocortisone	<6 h	Septic shock	PTSS-10	12 months	NS	LLLUHUH
Hoge et al. (2012)	USA	28	Propranolol	4–12 h	Physical injury	CAPS	3 months	NS	UUUUHUH
Kok et al. (2016)	Netherlands	2458	Dexamethasone	<6 h	Cardiac Surgery	PTSS-10	3 months	NS	LLLLLUH
Matsuoka et al. (2015)	Japan	110	Docosahexaenoic Acid	10 days	Injury	CAPS	3 months	NS	LLULLLL
Pitman et al. (2002)	USA	24	Propranolol	Less than 6 h	Injury	CAPS	3 months	NS	ULLUHHH
Schelling et al. (2001)	Switzerland	20	Hydrocortisone	Less than 6 h	Septic shock	PTSS-10	31 months	HC	ULLLHUH
Schelling, Kilger, Roozendaal, et al. (2004)	Switzerland	48	Hydrocortisone	Less than 6 h	Cardiac surgery	PTSS-10	6 months	HC	UHUHHUH
Stein, Kerridge, Dimsdale, and Hoyt (2007)	USA	38	Propranolol Gabapentin	Less than 48 h	Injury	PCL-C	4 months	NS	LLLLHLH
van Zuiden et al. (2016)	Netherlands	107	Oxytocin	6–12 h	Injury	CAPS	6 months	NS	LLLLLHH
Weis et al. (2006)	Germany	28	Hydrocortisone	Less than 6 h	Cardiac surgery	PTSS-10	6 months	NS	LLLLHUH
Zohar et al. (2011)	Israel	17	Hydrocortisone	Less than 6 h	Injury	CAPS	3 months	NS	LLLLHHH

[a] Risk of bias judgements for each study (in seven domains: A = random sequence generation; B = allocation concealment; C = blinding of participants/personnel; D = blinding of assessors; E = incomplete data F = selective reporting; G = other bias) are graded **L** = low risk; **U** = unclear risk; **H** = high risk).

individuals with a diagnosis of acute stress disorder which supports calls to detect and treat individuals with significant symptoms rather than providing blanket preventative interventions (McFarlane, 2010; Shalev, Gevonden, Ratanatharathorn, et al., 2019). Indeed, the results of the meta-analyses in this review suggest that the potential benefits of preventative interventions for individuals with only mild symptoms is questionable.

Stepped/collaborative care demonstrated a relatively stable finding of low, but positive, effect of efficacy. This is a key finding and the heterogeneity of different presentations and approaches within the studies included is likely to have diluted the results to a degree for the most effective approaches adopted. The finding suggests that assessing an individual's needs and appropriately matching interventions to these can be a helpful as well as a logical approach although more work is required to determine how best to achieve this. The efficacy signals found for brief EMDR, and internet-based guided self-help are also promising but need replication and one suspects attention to the optimal configuration and mode of delivery of these interventions needs more attention using methodology designed to do this (e.g., Moore et al., 2015).

Consistent with the results for cognitive interventions attempting to interfere with consolidation of the traumatic memory within a few hours of a traumatic event, the early use of various medications did not prevent PTSD. This is despite a strong mechanistic argument as to why

Table 11
Summary results of pharmacological intervention meta-analyses.

Intervention	Summary result versus TAU/WL (number of studies; number of participants; standardised mean difference and 95% confidence intervals)	GRADE judgment for quality of evidence
Hydrocortisone	k = 1; N = 43; SMD −0.63, CI −1.25 to −0.02	Very uncertain about the estimate.
Propranolol	k = 2; *N* = 52; SMD 0.06, CI −0.49 to 0.61	Very uncertain about the estimate.
Docosahexaenoic Acid	k = 1; *N* = 110; SMD 0.11, CI −0.26 to 0.49	Very uncertain about the estimate.
Oxytocin	k = 1; *N* = 107; SMD −0.24, CI -0.62 to 0.14	Very uncertain about the estimate.

some, e.g. propranolol, should work by reducing the initial adrenergic surge known to consolidate traumatic memories (Pitman, 2019). Hydrocortisone was the only pharmacological agent to provide emerging evidence of efficacy in preventing PTSD and interpretation of this needs to be very cautious given methodological issues and the fact that most studies have only been undertaken with seriously ill people to date, raising major questions around the generalizability of findings.

4.1. Strengths and limitations

The systematic review adhered to standard Cochrane Collaboration methodology. The focus was purely on PTSD and, therefore, other important outcomes such as depression and adverse effects were not considered. No attempt was made to conduct network meta-analyses which may have provided additional useful information. It is also noteworthy that treatment as usual, waitlist, or no treatment were grouped as comparators. Although a practice commonly adopted in meta-analyses, these comparators can be quite different and caution is required in interpretation as a result. It is important that any prevention strategy is better than natural recovery and it can, therefore, be argued that superiority over wait list/no intervention control is always required (McNally, Bryant, & Ehlers, 2003). The main limitation concerns the quality of the individual studies included. With a few notable exceptions, the review team had significant concerns around the methodology of individual studies resulting in judgements of significant risk of bias and lack of confidence in the efficacy estimates found in the meta-analyses conducted. Power issues were apparent in the vast majority of studies and it was unclear if interventions were always delivered consistently and with good fidelity.

4.2. Clinical implications

With the current evidence, it is difficult to argue that any intervention should be routinely delivered to prevent the development of PTSD. Given the strong evidence for the efficacy of treatments (psychological and to a lesser degree pharmacological) for diagnosed PTSD (Lewis et al., 2020; Hoskins et al., 2021) it seems most sensible to recommend that clinical practice should primarily focus on detecting individuals who are likely to have PTSD (or any other diagnosable condition) and treating them as soon as is feasible. With respect to preventative interventions, the evidence available suggests that individuals who develop symptoms are likely to benefit more from preventative interventions currently available than those who don't (i.e. indicated prevention is better evidenced than universal or selective prevention). The decision as to what level of symptoms are required before an intervention is given will probably depend more on resource availability than anything else. Evidence-informed approaches after traumatic events such as providing practical, pragmatic support in an empathic manner (Bisson et al., 2015), watchful waiting (NICE, 2018), providing information, emotional support and practical assistance (Phoenix Australia, 2020) or psychological first aid (WHO, 2011) remain appropriate, pending the development of more effective formal preventative interventions. These interventions may also serve as a first step in future stepped care approaches to address traumatic stress.

4.3. Research implications

There is clearly much research to be done with respect to both pre and post-trauma interventions to prevent PTSD. A number of interventions have emerging evidence of effect and it seems appropriate that a future research focus should be on their development and further evaluation. It will be important for future research to address the methodological weaknesses found in many of the trials included in the meta-analyses reported, including randomization generation and concealment, blinding of assessors, adequate sample sizes, fidelity checking, follow-up of longer term outcomes and full and complete reporting of data in line with a pre-study registered protocol.

A more detailed appraisal of intervention components that may or may not work, how best to deliver them and train people to do so should help the field to develop better novel and adapted approaches to PTSD prevention. Considering findings from discovery research and translating them into practice is one favored approach (Holmes, Craske, & Graybiel, 2014). A potential alternative and/or complementary approach is to undertake more in-depth modelling and piloting work to carefully develop and refine prototype intervention models so that those tested are optimally configured before being subjected to a feasibility RCT and then effectiveness trials (Craig et al., 2019). The preventative interventions identified as having emerging evidence of effect represent good candidates for such work, as do novel interventions informed by factors identified as being associated with a more positive outcome, such as trauma focus.

The studies included did not provide enough information to suggest that certain types of intervention may be best matched to particular people, for example as a result of specific characteristics, but considering this in more detail could inform intervention matching in the future and lead to a more personalized approach to the prevention of PTSD. The inclusion of Complex PTSD (CPTSD) as a sibling disorder to PTSD (WHO, 2018) opens up a new line of investigation, namely the prevention of CPTSD; given the recency of its development, there is a paucity of work on the prevention of CPTSD to date.

5. Conclusion

At present there is limited evidence to support blanket adoption of any approach to prevent PTSD. Some interventions have shown promise but at present the field is bedevilled by small, sub-optimally designed trials of likely sub-optimally configured interventions. We should be able to do better.

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